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Bangungut in Manila: sudden and unexplained death in sleep of adult Filipinos

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Background	Sudden and unexplained death in sleep (SUDS) is a leading cause of death of young men in several Asian populations, but the history and epidemiology of SUDS are not well known.
Methods	Autopsy records were reviewed in Manila in a study of the classification of SUDS. Death certificates filed in Manila during 1948–1982 were then reviewed in a study of SUDS incidence. A nested case-control study of death certificates examined birthplace as an indicator of SUDS risk.
Results	The classification of SUDS cases in Manila during 1948–1982 (N = 722) evolved from the folk term, *bangungut* ('to rise and moan during sleep'), to various descriptions of post-mortem artefacts. The characteristics of victims in each of the groups were similar: 96% male, mean age 33 years, and modal time of death 3:00 a.m. The deaths were seasonal, peaking in December-January. SUDS victims were more likely than deceased controls to have been born outside of the Manila region (relative odds = 2.11; 95% CI : 1.59–2.78). The SUDS rate for men aged 25–44 years increased from 10.8 to 26.3 per 100 000 person-years from 1948 to 1982.
Conclusion	The death certificate classification of SUDS in Manila has changed considerably, obscuring an increase in incidence. SUDS appears to be a regional phenomenon in Southeast Asia and environmental causes are likely because the deaths are seasonal, increased over the timespan studied, and are more common among migrants to Manila than among those born there.

Keywords	Sudden death, sleep, Southeast Asia, Philippines, surveillance, epidemiology
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A syndrome of sudden and unexplained death in sleep (SUDS) occurs among Filipino adults in the Philippines, Hawaii, Guam and the Marianas Islands,[1–11] Japanese,[12–14] Laotian, Cambodian, and Vietnamese refugees in Thailand and the United States,[15–28] and Thai men in Thailand and in Singapore.[29–38] The victims are typically young men, median age 30–34 years, all in apparent good health, who die within minutes of the onset of distress during sleep. The immediate cause of death is ventricular fibrillation, but in the absence of known disease.[19] Prolonged QT interval has been documented in electrocardiographic studies of Laotian-Hmong refugees at high risk of SUDS,[28] evidence that cardiac electrical instability may be a cause of SUDS, but the underlying mechanisms are unclear. Proposed causes of SUDS include thiamine deficiency,[27–28] hypokalaemia,[29,32] nightmares and mental stress,[1–9,16–18,23,26,34,39,40] melioidosis,[37] and genetic factors.[33] No evidence directly links the sudden deaths of Asian adults with sudden deaths of infants that also occur in sleep. While SUDS is known to occur in many populations in Asia, its history, boundaries and incidence are not well known. The highest known rate of SUDS was documented among refugees from Laos and Cambodia in refugee camps in Thailand.[20] Southeast Asian refugee men who resettled in the US after 1975 arrived with a high susceptibility to SUDS but the risk dropped sharply with increasing length of residence in the US.[25]

SUDS was first described in the medical literature of the Philippines in 1917[1] and these deaths were popularly known there as *bangungut*—a Tagalog word meaning 'to rise and moan in sleep'. Similar deaths were noted in the late 1940s and 1950s in Hawaii among Filipino migrant labourers and were widely discussed in the Filipino medical literature.[2–10] *Bangungut* deaths are now widely attributed to 'acute haemorrhagic pancreatitis' by medical personnel in the Philippines despite evidence that the pancreatic changes emphasized in this classification are artefacts of post-mortem autolysis.[9]

Sudden deaths in sleep of healthy young adults mostly occur out of hospitals and are usually investigated where medical-legal systems exist. The widespread practice of autopsy in cases of unexplained death in Manila after World War II, uncommon

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in most other parts of Asia, allowed an unusual opportunity for epidemiological study. In this paper we describe the history of classification of sudden deaths in sleep in Manila that remained unexplained after autopsy. With this nosology, a sample of death certificates was then reviewed to allow a description of the epidemiology of SUDS in Manila between 1948 and 1982.

Methods

Review of autopsy reports of sudden deaths in Manila

Autopsy reports of sudden deaths investigated between 1952 and 1982 by the Medical-Legal Division of the Manila Police Department were available for review. Reports of cases from every fourth year between 1952 and 1980 and in 1981–1982 were reviewed to look for evidence of a distinct subgroup of sudden deaths that occurred in sleep and to document the assigned causes of death. A sudden death was defined as a death within 24 hours of the onset of acute signs or symptoms in a previously healthy individual.[41] Deaths due to accident, homicide, suicide, poisoning, or drowning were excluded from further consideration. Acute haemorrhagic pancreatitis, a popular explanation for SUDS in the Philippines[9] was not accepted as an adequate cause of sudden death unless there was evidence of a clear clinical course before death.

We constructed a comprehensive definition of SUDS in Manila by noting the officially assigned causes of sudden death in cases that remained unexplained after autopsy in which the circumstance of death in sleep were mentioned in the autopsy report; these classifications of cause of death appeared to be specific for SUDS cases, thus were used as presumptive case definitions of SUDS in a systematic review of death certificates.

Review of death certificates in Manila

All death certificates filed in the Manila Health Department every fourth year between 1948 and 1980 and between 1 August 1981 and 31 July 1982 were reviewed in a broader study of the epidemiology of SUDS in Manila. Data on age, gender, date and time of death, birthplace, residency and autopsy status were abstracted from the death certificates. The certified causes of death were grouped into similar categories and the characteristics of victims in each group were compared to see whether or not they were homogeneous.

Demographic data on the Manila population were obtained from the Philippines National Bureau of Census and Statistics for the census years of 1939, 1960, 1970 and 1975. Data on total population size of Manila for each sample year were available from the Manila Health Department. Estimates of the age-distributions by sex for the sample years studied were derived by interpolation between census years. Residency data were not collected on cases from 1952, 1960, 1968 and 1976; for these years the proportions of cases that were Manila residents were estimated by interpolation between the known residency rates of cases in the other sample years. Estimates of age-specific SUDS rates for 5-year age groups of men for all sample years combined were calculated by summing the known and estimated numbers of cases of SUDS among male residents of Manila in each age group across all sample years and dividing by the summed person-years accumulated by resident men in each age group in Manila for the same years. Age-adjusted death rates by year for resident men of Manila were estimated using the direct method[42] and the estimated 1968 population structure of Manila as the standard population.

Case-control study of migration and risk of SUDS

In the study of migration and risk of SUDS, controls were selected from death certificates and matched by gender and age to SUDS cases from the following sample years: 1948, 1956, 1964, 1972, 1980 and 1981–1982. Controls were not matched to abstracted cases from 1952, 1960, 1968 and 1976 because of limited resources. The deceased controls were identified by selecting the next death certificate filed after a case that was of the same sex and within 3 years of the case's age, and in which death was due to a cause other than SUDS.

In the analysis of location of birth and residence, provinces were grouped into the following geographical regions: northern Luzon, central Luzon, southern Luzon, Visayan, Mindanao and the Manila region. The Manila region was defined as the city of Manila, the metropolitan Manila area, and the nearby provinces of Pampanga, Rizal, Bulacan, Laguna, Bataan and Cavite. The relative odds of birth in each region outside of the Manila region versus birth in the Manila region for cases compared to controls and the 95% confidence intervals were calculated.

Results

Classification of SUDS deaths in Manila autopsy reports

Autopsy reports of 382 sudden deaths were reviewed and grouped into four broad categories including (1) unexplained after autopsy (48%), (2) myocardial infarction (38%), (3) other and ill-defined heart disease (11%), and (4) rheumatic heart disease (2%) (Table 1). The mean age of victims of death that was unexplained after autopsy was 33.5 years and 97% were male. Victims of myocardial infarction and 'other and ill-defined heart disease' were older (mean age 54.0 and 45.2 years respectively) and fewer were male. Death in sleep was mentioned in the descriptive portion of the autopsy reports of 62% of the unexplained deaths, 4% of the myocardial infarction deaths, and in none of the deaths due to 'other and ill-defined heart

Table 1 Classification of cause of death after autopsy and selected characteristics of 382 sudden deaths of adults occurring during 1952–1982 in Manila, and selected characteristics of each group

Classification	No. (%)	Death in sleep (%)[a]	Mean age (SD)	% male
Unexplained after autopsy	183 (48)	62	33.5 (10)	97
Myocardial infarction	147 (38)	4	54.0 (13)	85
Other and ill-defined heart disease	43 (11)	0	45.2 (18)	74
Rheumatic heart disease	9 (2)	0	37.5 (19)	33

[a] Death in sleep mentioned in the autopsy report.

Table 2 Certified cause of death and selected characteristics of 722 cases of sudden and unexplained death in sleep (SUDS) in Manila during 1948–1982

Certified cause of death	No.	Mean age in years (SD)	% male	Mode time of death	Autopsy rate (%)
Acute cardio-respiratory failure (ACRF)—*bangungut* type	81	33 (9)	98	4:00 a.m.	98
ACRF with congestion and petechial haemorrhages of internal organs	168	34 (10)	96	3:00 a.m.	99
ACRF in sleep	98	30 (8)	99	2:00 a.m.	100
ACRF with acute haemorrhagic pancreatitis	73	33 (11)	97	4:00 a.m.	85
Acute haemorrhagic pancreatitis	225	33 (11)	98	1:00 a.m.	91
Pending	77	32 (13)	86	1:00 a.m.	99
All SUDS deaths	722	33 (10)	96	3:00 a.m.	95

Table 3 Distribution of death certificate classifications by year of sudden and unexplained deaths in sleep (SUDS) in Manila: 1948–1982

	Per cent of all cases in a given year									
Certified cause on death certificate	1948 N = 27	1952 N = 23	1956 N = 53	1960 N = 60	1964 N = 50	1968 N = 75	1972 N = 78	1976 N = 100	1980 N = 107	1982 N = 149
Acute cardio-respiratory failure (ACRF)—*bangungut* type	29.6	69.6	60.4	8.3	6.0	4.0	1.3	10.0	7.5	0.0
ACRF with congestion and petechial haemorrhages of internal organs	37.0	13.0	18.9	33.3	30.0	56.0	23.1	19.0	9.3	8.7
ACRF in sleep	0.0	0.0	0.0	8.3	8.0	4.0	39.7	39.0	4.7	6.7
ACRF with acute haemorrhagic pancreatitis	18.5	0.0	11.3	40.0	24.0	4.0	5.1	10.0	0.9	7.4
Acute haemorrhagic pancreatitis	3.7	17.4	9.4	8.3	18.0	30.7	16.7	6.0	68.2	56.4
Pending	11.1	0.0	0.0	1.7	14.0	1.3	14.1	16.0	9.3	20.8

disease' or rheumatic heart disease. Victims of sudden death attributed to rheumatic heart disease were relatively young (mean age 37.5 years) and two-thirds were women. The deaths due to 'other and ill-defined heart disease' included hypertensive heart disease (N = 2), pericarditis (N = 3), heart failure (N = 18), cardiomegaly (N = 16), and ill-defined heart disease (N = 4).

Sudden deaths that remained unexplained after autopsy and that were documented as occurring in sleep had the following certified causes of death: (1) acute cardiorespiratory failure—*bangungut* type, (2) acute cardiorespiratory failure with congestion and petechial haemorrhages of internal organs, (3) acute cardiorespiratory failure in sleep, (4) acute cardiorespiratory failure with acute haemorrhagic pancreatitis, and (5) acute haemorrhagic pancreatitis. Deaths listed in these five groups were considered SUDS deaths and studied in more detail in the review of death certificates.

SUDS cases among Manila death certificates

A total of 147 676 death certificates were reviewed for the 10 sample years between 1948 and 1982 in a search for SUDS cases. Early in the review, a sixth group likely to contain cases of sudden death in sleep was found: cases autopsied by the Philippine National Bureau of Investigation with the cause of death listed as 'pending'. Data from all 'pending' deaths were also abstracted.

Characteristics of 722 cases found in the six SUDS groups are listed in Table 2. For all cases combined, the mean age was 33 years, the age range was 13–77 years, 96% were men, the mode time of death was 3:00 a.m. and the autopsy rate was 95%. Manila residents accounted for 70% of these cases. The six groups of SUDS deaths each had similar characteristics so these were combined and considered as a comprehensive definition of SUDS for further analyses.

The percentage of cases that were autopsied in the six groups ranged from 85% to 100% and overall the rate did not vary significantly by year. Autopsies of the cases were performed by the Medical-Legal Division of the Manila Police Department (76%), the Philippine National Bureau of Investigation (19%), local hospitals (4%), and the Philippine Constabulary (1%). The mean age and sex of cases autopsied in different institutions were similar (data not shown).

The numbers of SUDS cases by year in each of the six classifications are shown in Table 3. While some overlaps in these classifications existed over time, a clear evolution in classification occurred between 1948 and 1982. The common Tagalog classification, *bangungut*, was used in combination with 'acute cardiorespiratory failure' (ACRF) in 69.6% of the cases in 1952 but it fell out of favour as an acceptable certified cause of death by 1960 when it accounted for only 8.3% of cases. A description of non-specific pathology found at autopsy including congestion, oedema, and petechial haemorrhages of internal organs commonly appeared on the death certificate in combination with ACRF in 1948 (37.0%), declined to 13.0% in 1952, then increased until 1968 when it accounted for 56.0% of cases. As early as 1948 acute haemorrhagic pancreatitis (AHP) was used alone (3.7%) or in combination with ACRF (18.5%) and by 1980 AHP alone was used to classify 68.2% of the SUDS cases.

The SUDS cases for all sample years combined were seasonal, with a peak in the December-January period (Figure 1). This distribution was significantly different from all other deaths in Manila ($\chi^2 = 59.4$, d.f. = 5, $P < 0.001$). The peak period of SUDS occurred during the nadir of the distribution of all other Manila deaths.

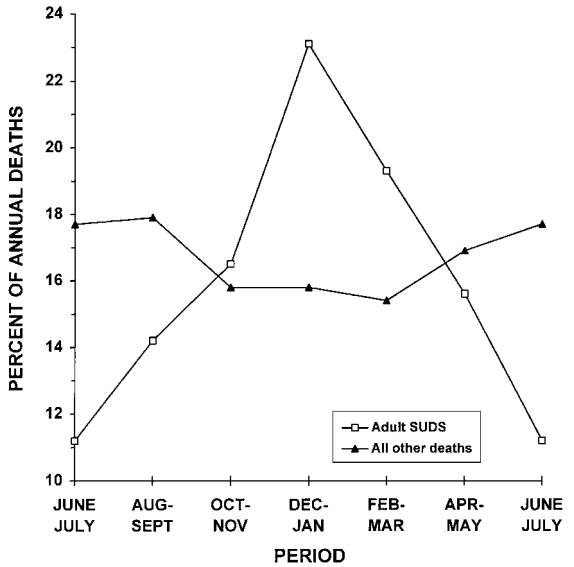

Figure 1 Seasonality of sudden and unexplained deaths in sleep (SUDS) of adults and all other deaths combined in Manila for all sample years, 1948–1982

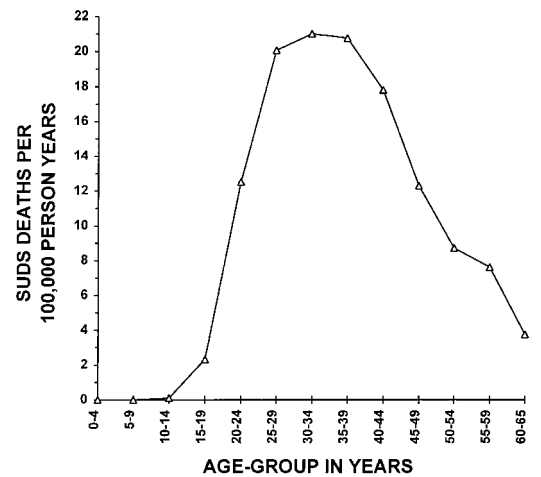

Figure 2 Rates of sudden and unexplained death in sleep (SUDS) of male residents of Manila by age group: all sample years combined, 1948–1982

The age-specific rates of SUDS for Manila men in all years combined are shown in Figure 2. The death rate rises ninefold (from 2.3 to 21.0 per 100 000 person-years) from age groups 15–19 years to 30–34 years, then markedly declines with increasing age.

The age-adjusted rates of SUDS by year among resident Manila men are shown in Figure 3. These rates were calculated for men aged 25–44 years only to minimize the misclassification of SUDS cases that may be more likely at younger and older ages. Separate rate estimates were made with and without the 'pending' group of cases. Addition of the pending cases slightly raised the rate estimates after 1968. With the pending cases

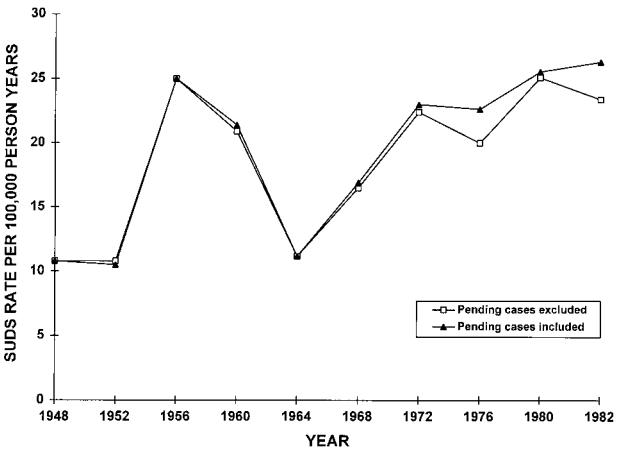

Figure 3 Age-adjusted rates of sudden and unexplained death in sleep (SUDS) in Manila men aged 25–44 years, 1948–1982

excluded, the death rate per 100 000 person-years increased 2.2 fold from 1948 to 1981–1982 (from 10.8 to 23.4); with the pending cases included, the rate increased 2.4 fold over the same period (from 10.8 to 26.31).

Case-control comparison of migration and risk of SUDS

In both the group of 722 SUDS cases and the 454 controls the mean age at death was 33 years and 96% were male. The percentages of cases and controls listed as Manila residents were similar (70%). SUDS cases were twice as likely as controls to have been born outside of the Manila region (OR = 2.11, 95% CI : 1.59–2.78). The odds ratios contrasting birthplace in areas outside of the Manila region with birth in the Manila region for cases compared to controls are shown in Figure 4. The relative odds of birth outside of the Manila region for cases compared to controls increased when birth regions progressively further from Manila were considered. Cases were 4.4 times more likely than controls (95% CI : 1.35–12.42) to have been born on Mindanao, a large island that is the furthest south from Manila. Seven of the SUDS victims were born in China and later migrated to the Philippines and became Filipino citizens; none of the controls had this history (Fisher's exact test, $P = 0.02$).

Discussion

Bangungut was first used in the published medical literature in the Philippines by Guazon in 1917[1] to describe sudden and unexplained death in sleep of young Filipino men. Most of the published reports of SUDS in the Philippines have included mention of *bangungut* in their titles. *Bangungut* is still commonly used by medical personnel and lay people in the Philippines to describe SUDS. In fact, since 1982 we have informally queried scores of Filipino health professionals and lay people about *bangungut* and each has described the deaths in a similar way and has known of one or more relatives or acquaintances who died under these circumstances. *Bangungut* was commonly used on death certificates in combination with 'acute cardiorespiratory failure' (ACRF) through the mid-1950s, but the usage

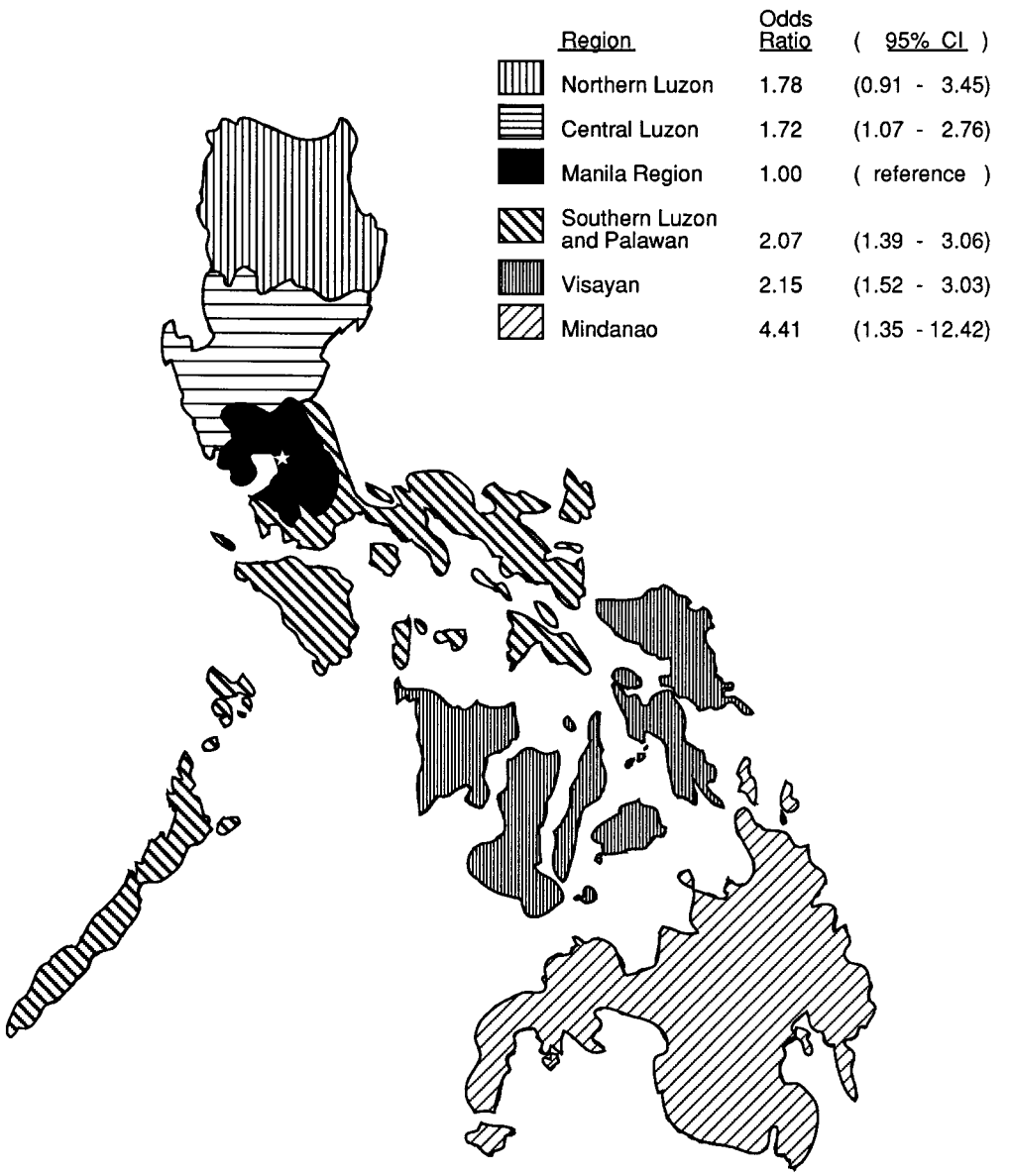

Figure 4 Relative odds of birth outside of the Manila region among victims of sudden and unexplained death in sleep (SUDS) in Manila vs. deceased controls in Manila; 1948–1982

declined after that and medical jargon took its place. Death certificates listing ACRF in sleep became embellished with long descriptions of non-specific pathological findings including congestion, oedema, and petechial haemorrhages of internal organs. Curiously, the condition of the pancreas became emphasized in the listed cause of death and SUDS deaths are now commonly known by medical personnel in the Philippines as 'acute haemorrhagic pancreatitis' in spite of the fact that no evidence exists of a pancreatic condition preceding the deaths.[9] The classification of SUDS in the Philippines has thus evolved from a Tagalog folk term to modern medical jargon, and this has obscured the importance of SUDS in vital records and the increase in the rate of SUDS from 1948 to 1982.

The characteristics of SUDS victims in each of the death certificate classifications described in our study are the same and did not change appreciably over the 34-year period studied: the highest risk was among men 30–34 years of age. The similarity of the mean age of SUDS victims (30–34 years) in all the Asian populations studied is striking. Most of these populations are from less developed countries and the relatively young age at death could be an artefact of large numbers of young men in the population. The Manila study confirms that the actual risk of sudden death in sleep among Filipino men rises sharply to a peak at 30–34 years, then declines with increasing age. This age distribution appears to be a characteristic feature of SUDS in Asia and may provide clues to mechanisms related to cardiac

arrhythmias and sleep disorders in the absence of atherosclerotic heart disease. A similar peak in the risk of sudden death may exist among Western populations, hidden beneath a larger burden of sudden death associated with atherosclerotic disease that increases in incidence with advancing age.

The pattern of SUDS is also well known among Japanese as *pokkuri* disease and has been described among Southeast Asian refugees in Thailand and the US and in Thai villagers and labourers, among whom it is known as *lai tai* (sleep-death). The epidemiological profile of the deaths is remarkably similar in each of these Asian populations: average age 30–34 years, age range 15–65 years, a strong male predominance, almost instantaneous death in sleep of an individual thought to be previously healthy, and lack of known cardiovascular disease. The sudden deaths in sleep of Asian adults are different from major patterns of sudden death known in Western populations. Among adults in the West, sudden death is strongly associated with atherosclerotic heart disease, is not associated with sleep, and is more likely to occur with increasing age.[43–46]

SUDS rates have declined markedly among Southeast Asian refugees in the US with their increasing length of residence,[25] implicating some aspects of their impoverished lifestyle in Asia. *Pokkuri* disease is generally thought to have declined in Japan in the post-World War II era. We expected to also find a decline in SUDS rates in Manila with the increasing modernization and improving health profile of the population since World War II, but we found quite the opposite: the rate of SUDS fluctuated but generally increased in Manila between 1948 and 1982. The observed rate of SUDS in Manila may have become spuriously elevated over time with an increase in case-finding or an increase in the misclassification of deaths related to other causes; these explanations however, seem unlikely. For an artefact of increased case-finding in more recent years to have been important, cases in the earlier period would have to have been undetected. The overall rise in rates is not due to the definition of new categories of sudden death classification; all were in use by 1964, the year in which the strong and sustained increase in SUDS death rates began. The rate of autopsy was consistently high throughout the period of study for each of the categories of classification. The demographic characteristics of cases in each of the categories of classification and for all cases over the period of study were also similar, lending credence to the view that the SUDS deaths we defined were homogenous across the commonly used classifications and over time.

The high rate of autopsy in Manila of cases of sudden death is rare elsewhere in Asia, with the exception of Singapore,[34] and the autopsies added assurance that the SUDS cases in Manila were accurately classified. The validity of the individual autopsy findings was not addressed in this study however. The direction of misclassification might be expected to be towards more often 'explaining' more recent deaths due to new diagnostic methods or disease theories and thus an increasing underestimation of SUDS death rates over time. The shift in classification of sudden deaths in sleep to 'acute haemorrhagic pancreatitis', if it had not been detected in our study and shown to be similar to other sudden deaths in sleep, would have resulted in a loss of cases and a spurious conclusion that the death rates had decreased since 1976. While detailed post-mortem studies were not completed in the past, the high rate of autopsy in Manila would provide a good opportunity for future studies of the pathology of SUDS.

SUDS is such a striking phenomenon that little misclassification would be expected from case definitions based, in the absence of autopsy, on the circumstances of death and external examinations of the bodies of victims[20,23,33–35] and inclusion of each of the following: (1) death within minutes or hours of the abrupt onset of agonal signs in a previously healthy individual; (2) no external evidence of violence, accident, drowning, asphyxiation or drug overdose; (3) death associated with nighttime sleep, day-time nap, or the transition between sleep and wakefulness; (4) an age range of victims restricted to that of peak incidence (such as 25–44 years) to avoid misclassification of deaths at younger and older ages that might be due to other causes. This 'presumptive' definition of SUDS should not be limited to men or nocturnal events. The definition of SUDS based on these circumstances should be adequate to describe SUDS occurrence in populations with a high incidence and few or no autopsies, but will be less adequate in low-risk populations in which a higher proportion of sudden deaths may be due to other mechanisms including epilepsy, cardiac electrical instability with other origins,[47] drug overdose or other causes.

Short-term fluctuations in the rate of SUDS may have occurred in Manila in the period studied, but we had a limited ability to define these since we sampled death records at 4-year intervals. In 1956 the death rate for men 25-44 years rose to a level equivalent to the 1980 rate, then declined over the next 8 years. In 1956 the mayor of Manila created a commission on *bangungut*, a *bangungut* research foundation was formed, and the Philippine Medical Association held a symposium on *bangungut*.[48] More sampling of Manila deaths in this period may indicate whether or not fluctuations in death rates occurred in synchrony with environmental changes or population movements and whether the increased civic awareness was an effect of increased SUDS incidence or a social phenomenon that led to an increased awareness and diagnosis of SUDS. The observed rise over time in rates of sudden death in sleep in Manila could have been due to an increase in the susceptibility of individuals due to environmental changes or a migration of impoverished, susceptible individuals into Manila from rural areas. A comparison of residency of SUDS cases and controls revealed no significant differences—70% of each were listed as Manila residents. This may not be a useful definition because residency status is attained after only 6 months in Manila. The analysis of birthplace revealed that cases were more likely than controls to have been born outside the Manila region. This relationship appeared stronger when birth regions progressively further south from Manila were considered. The case-control comparison must be interpreted with caution because the controls were selected from death certificates. Controls who died at this relatively young age, whether from disease, accidents, or violence may not be representative of the general population, but the results of this comparison are similar to more recent studies of Southeast Asian refugees[25] indicating that recent migrants have an increased risk of SUDS compared to immigrants who have settled for a longer period of time.

The occurrence of SUDS in Asian populations that are culturally and genetically distinct, the elevated risk among migrants to Manila, the seasonal occurrence, and the sharp decline in SUDS incidence among Southeast Asian refugees after immigration to the US all provide evidence that environmental factors in Asia play a major role in this unexplained syndrome. The most

plausible causes of SUDS are regional environmental and nutritional factors common among the poor of Southeast Asia (and formerly Japan) that span the various cultures of this area. The Philippines is a country rich in cultural and environmental diversity and has an appreciable number of SUDS cases, thus is well suited for aetiologic studies of sudden death in sleep.

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